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TITLE: Apo-A-I regulation of T-cell signaling

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INVENTOR-INFORMATION:

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US-CL-CURRENT: 435/69.1, 424/145.1 , 435/320.1 , 435/326 , 530/388.23
, 536/23.53

ABSTRACT:

The invention provides AFTI polypeptides and nucleic acid molecules encoding
the same. The invention also provides vectors, host cells, selective binding
agents, and methods for producing AFTI polypeptides. Also provided are methods

for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI
polypeptides, particularly IL-1 mediated diseases, TNF-.alpha. mediated
diseases, and diseases involving monocyte activation.

[0001] This application claims the benefit of U.S. Provisional Application No.
60/189,008, filed Mar. 13, 2000 and of U.S. Provisional Application No.
60/193,551, filed Mar. 31, 2000, both of which are hereby incorporated by
reference herein in their entirety for any purpose.

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Summary of Invention Paragraph - BSTX (59):
[0056] FIG. 1: (A) Human apolipoprotein A-I amino acid sequence (SEQ ID
NO:2) and polynucleotide sequence (SEQ ID NO:1). Apo A-I polypeptide has
helical lipid binding domains (amino acid residues 44-65 and 220-241), a domain
involved in lipoprotein-mediated cholesterol efflux from monocytes (amino acid
residues 74-111), a receptor binding domain (amino acid residues 149-219), a
major antigenic epitope domain (amino acid residues 99-120), a hinged domain
(amino acid residues 99-143), a phylogenetically conserved domain (amino acid
residues 66-120), and a domain involved in lectin-cholesterol acyltransferase
acitivity (amino acid residues 90-111). The apo-A-I polypeptide has eight
amphipathic helices (amino acid residues 44-65, 66-98, 99-120,121-142,143-164,
165-208, 209-219, 220-241), an N-terminal peptide (amino acid residues 1-43),
and a C-terminal peptide (amino acid residues 242-243). AFTI amino acid
sequences include, but are not limited to, fragments of SEQ ID NO:2, for
example, (B) a 18 kDa N-terminal fragment (amino acid residues 25-194,
nucleotides 92-601), (C) a 13 kDa N-terminal fragment (amino

acid residues
25-144, nucleotides 92-451), and (D) a 13 kDa C-terminal fragment (amino acid
residues 156-267, nucleotides 485-820).

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TITLE: Orally administered peptides to ameliorate atherosclerosis

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INVENTOR-INFORMATION:

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US-CL-CURRENT: 514/12, 514/13 , 514/14 , 514/15 , 530/324 , 530/325 , 530/326 , 530/327

ABSTRACT:

This invention provides novel peptides that ameliorate one or more symptoms of atherosclerosis. The peptides are highly stable and readily administered via an oral route.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No.
09/645,454, filed on Aug. 24, 2000, which is incorporated herein by reference
in its entirety for all purposes.

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Detail Description Paragraph - DETX (155):
[0183] Plasma levels of high density lipoproteins (HDL) and apolipoprotein
A-I (apo A-I), the major protein constituent of HDL, are inversely correlated
to coronary artery disease (CAD) (Sprecher et al. (1993) Arterioscler. Thromb.
13: 495-504; Philips et al (1993) Circulation 88: 2762-2770). Human apo A-I is
a 243 residue protein, containing eight 22-mer amphipathic helical repeats, the
majority of which have been shown to possess the Class A motif (Segrest et al.
(1990) Proteins 8: 103-117; Anantharamaiah et al. (1993) pp. 109-142 In: The
Amphipathic Helix (Epand, R. M., ed), CRC Press, Boca Raton, Fla.). Class A
amphipathic helices have a characteristic charge distribution; they have a
cluster of positively charged amino acids at the polar/nonpolar boundary of the
.DELTA. helix and negatively charged residues at the center of the polar face
(Segrest et al. (1990) Proteins 8: 103-117; Anantharamaiah et al. (1993) pp.
109-142 In: The Amphipathic Helix (Epand, R. M., ed), CRC Press, BocaRaton,
Fla.; Segrest et al. (1992) J. Lipid Res. 33: 141-166). This unique secondary
structural motif has been postulated to be responsible for the
lipid-associating property of apo A-I (Segrest et al. (1990) Proteins 8:
103-117). Many studies with synthetic analogues of Class A amphipathic helices
have supported this concept (Segrest et al. (1994)Adv. Prot.

Chem., 45:
303-369; Brouillette and Anantharamaiah (1995) Biochim. Biophys. Acta 1256:
103-129). Recently, we have synthesized each of the putative 22 mer helices
present in human apo A-I as monomers and tandem dimers and shown that the N-
and C-terminal amphipathic helices possess the maximum lipid-associating
ability (Mishra et al. (1998) Biochemistry 37: 10313-10324). X-ray crystal
structure and molecular modeling studies of the exon 4 (44-243 residues) of apo
A-I suggests that a self-associated state of the entire apo A-I is necessary
for lipid association (Borhani et al. (1999) Proc. Natl. Acad. Sci. USA.
94:12291-12296; Segrest et al. (2000) Current Opin. Lipidol. 11:105-115). In
this model, two molecules of apo A-I are arranged in the form of a head-to-tail
dimer with the monomers interacting with each other to stabilize the
lipid-associated structure of apo A-I.